

In the Specification:

Please amend the specification as shown:

Please delete paragraph [0065] and replace it with the following paragraph:

[0065] Figure 2 is a photograph of the gel representing the quantitative course of the cleavage of the modified oligonucleotide, wherein from left to right:

1. 5'-TTG ACG GTA TAT CT-3' (SEQ ID NO: 3) (14mer control) + dye (XC + BP);
2. 5'-AGC CCT TAC T-3' (SEQ ID NO: 2) (10mer control);
3. Model oligonucleotide 5'-AGC CCT TAC TTT GAC GGT ATA TCT-3' (SEQ ID NO: 1 or 4);
4. Empty;
5. Model oligonucleotide (unmodified);
6. Cleavage reaction;
7. Cleavage reaction;
8. Model oligonucleotide (unmodified);
9. Cleavage reaction;
10. Cleavage reaction;
11. Model oligonucleotide (modified P-S bond);
12. Cleavage reaction;
13. Cleavage reaction;
14. Model oligonucleotide (modified P-S bond);
15. Cleavage reaction; and
16. Cleavage reaction.

Please delete paragraph [0248] and replace it with the following paragraph:

[0248] Example 2:

Synthesis of a model oligonucleotide 5'-AGC CCT TAC TTT GAC GGT ATA TCT-3' (SEQ ID NO: 1 or 4)

Please delete paragraph [0256] and replace it with the following paragraph:

[0256] 15 μ l of a 50 mM silver nitrate solution are added to 1 O.D. of the model oligonucleotide and the solution is allowed to stand for 1 h at room temperature. The reaction is quenched by adding 4 μ l of a 220 mM DTT solution. After 1 h, the sample is centrifuged and the solution is removed. HPL chromatography and gel electrophoresis (15% TBE/urea gel, 1.0 mm x 15 well, 250 V, 90 min) follows for analytical purposes. The fragments formed during the cleavage

5'-AGC CCT TAC T-3' (SEQ ID NO: 2) (10mer)

5'-HO-TT GAC GGT ATA TCT-3' (SEQ ID NO: 3)
(14mer)

and the unmodified oligonucleotide

5'-AGC CCT TAC TTT GAC GGT ATA TCT-3' (SEQ ID NO: 1 or 4)

are used as controls.

Please delete paragraph [0260] and replace it with the following paragraph:

[0260] The retention times of the oligonucleotides are summarised in the following Table:

5'-TTG ACG GTA TAT CT-3' (<u>SEQ ID NO: 3</u>)	24.26 min
---	-----------

5'- AGC CCT TAC T-3' <u>(SEQ ID NO: 2)</u>	23.22 min
5'-AGC CCT TAC TTT GAC GGT ATA TCT-3' <u>(SEQ ID NO: 1 or 4)</u>	28.42 min
Cleavage reaction carried out	23.49 min; 24.65 min

Please delete paragraph [0262] and replace it with the following paragraph:

[0262] As a further analytical procedure, a measurement was run on a Biacore device (Uppsala, Sweden) in order to indicate that the cleavage is possible also on a solid phase. The following oligonucleotide was synthesised for these measurements:

5'-biotin-AGC CCT TAC TTT GAC GGT ATA TCT-3' (SEQ ID NO: 1 or 4)

Please delete paragraph [0263] and replace it with the following paragraph:

[0263] The 5'-end of the oligonucleotide was biotinylated (Glen Research, Sterling, Virginia, USA). The synthesis of the oligonucleotide is performed as described in Example 2. Further modification at the 5'-end was carried out on an Applied Biosystem 394 synthesizer. For the synthesis, a standard cycle was applied whose coupling time was extended to 300 s. Purification and processing also took place as described in Example 2. Moreover, three oligonucleotides were synthesised for the measurements, which exhibit different complementary regions with the modified model oligonucleotide. These three compounds, which were synthesised and purified according to standard conditions, are as follows:

1. 5'-GCA GCT AGA TAT ACC GTC AA-3' (SEQ ID NO: 5)

2. 5'-GCT AGA TAT ACC GTC AAA GT-3' (SEQ ID NO: 6)

3. 5'-GAT ATA CCG TCA AAG TAA GG-3' (SEQ ID NO: 7)

5'-AGC CCT TAC TTT GAC GGT ATA TCT-3' (SEQ ID NO: 1 or 4)

(1.) 3'-AA CTG CCA TAT AGA TCG ACG-5' (SEQ ID NO: 5)

(2.) 3'-TG AAA CTG CCA TAT AGA TCG-5' (SEQ ID NO: 6)

(3.) 3'-GGA ATG AAA CTG CCA TAT AG-3' (SEQ ID NO: 7)

Please delete paragraph [0266] and replace it with the following paragraph:

[0266] For binding to a chip, the following oligonucleotides were synthesised:

5'-amino-AGC CCT TAC TTT GAC GGT ATA TCT-3' (SEQ ID NO: 1 or 4)

5'-amino-AGC CCT TAC TTT GAC GGT ATA TCT-3' (SEQ ID NO: 1 or 4) (control sequence)

Please delete paragraph [0299] and replace it with the following paragraph:

[0299] After determining the probe sequence, these are produced synthetically as illustrated e.g. in Example 2. The sequences of the probes are indicated in the following Table.

Application No.: 10/789,081

Docket No.: MAIWAL 3.9-002 CONT

1	TCTAAAACCTGGCCAGCAATCATTC <u>(SEQ ID NO: 8)</u>	3'Cy3	5'NH2 phosphothio ate
2	GCCCCGGGCATTTCTCTCATTAACAT <u>(SEQ ID NO: 9)</u>	3'Cy3	5'NH2 phosphothio ate
3	TTCGAAAAGATTGCCTCCACATCAG <u>(SEQ ID NO: 10)</u>	3'Cy3	5'NH2 phosphothio ate
4	GTCTCATCTTTCTTCACGGAGCTGC <u>(SEQ ID NO: 11)</u>	3'Cy3	5'NH2 phosphothio ate
5	TGCTTGTTTGCTCTGTTCCTTTTCA <u>(SEQ ID NO: 12)</u>	3'Cy3	5'NH2 phosphothio ate
6	TCCAGGTTTTCCAGGAGAGAATCCA <u>(SEQ ID NO: 13)</u>	3'Cy3	5'NH2 phosphothio ate
7	TCTGGGTCAGCTCCTTCTTAATGGC <u>(SEQ ID NO: 14)</u>	3'Cy3	5'NH2 phosphothio ate
8	TCTAGAGGATGCATTTGACATGCCA <u>(SEQ ID NO: 15)</u>	3'Cy3	5'NH2 phosphothio ate
9	TGTTACATTTGTGTTGAACTGCCCC <u>(SEQ ID NO: 16)</u>	3'Cy3	5'NH2 phosphothio ate
10	AATGAGATTGCCTTTGCAGTTAGGG <u>(SEQ ID NO: 17)</u>	3'Cy3	5'NH2 phosphothio ate
11	TTCTTTTGCCCTAGCTCCAAGTTCA <u>(SEQ ID NO: 18)</u>	3'Cy3	5'NH2 phosphothio ate
12	TCGTCCAACAAATACTTTGCGATCA <u>(SEQ ID NO: 19)</u>	3'Cy3	5'NH2 phosphothio ate
13	AATAGCTCTTTCAGCTGCTTCCTGC <u>(SEQ ID NO: 20)</u>	3'Cy3	5'NH2 phosphothio ate
14	TACAAATCCATAGCCCTTGGAACCA <u>(SEQ ID NO: 21)</u>	3'Cy3	5'NH2 phospho- thioate
15	TATGTTGCCTACTCCACTTTTGCGA <u>(SEQ ID NO: 22)</u>	3'Cy3	5'NH2 phospho- thioate
16	TGTTCAAATTTGCGCTTAAGTTCCG <u>(SEQ ID NO: 23)</u>	3'Cy3	5'NH2 phospho- thioate

17	TTTGTTTTCCATTGAGCTCCTTTCC <u>(SEQ ID NO: 24)</u>	3'Cy3	5'NH2 phospho- thioate
18	TTACTTTCACACTTAAGGCAGGCCC <u>(SEQ ID NO: 25)</u>	3'Cy3	5'NH2 phospho- thioate
19	GACATGACTCGTGGAACCTGTGAAG <u>(SEQ ID NO: 26)</u>	3'Cy3	5'NH2 phospho- thioate
20	TAAATGGTGGTCTAGGAGCAGCTGG <u>(SEQ ID NO: 27)</u>	3'Cy3	5'NH2 phospho- thioate
21	TTGGCTAGGAGGATAGTATGCAGCA <u>(SEQ ID NO: 28)</u>	3'Cy3	5'NH2 phospho- thioate
22	AACACAGCGTGTTGCTAACACATCA <u>(SEQ ID NO: 29)</u>	3'Cy3	5'NH2 phospho- thioate
23	CTGTCCGCACCGTTCCACAGTATAA <u>(SEQ ID NO: 30)</u>	3'Cy3	5'NH2 phospho- thioate
24	CAGCAACATCTTAATGCACAGCCAC <u>(SEQ ID NO: 31)</u>	3'Cy3	5'NH2 phospho- thioate
25	AAGTTACAATGCAACAGCCTGCTGT <u>(SEQ ID NO: 32)</u>	3'Cy3	5'NH2 phospho- thioate
26	TCTAAAACCTGGCCAGCAATCATTCTGCCA <u>(SEQ ID NO: 33)</u>	3'Cy3	5'NH2 phospho- thioate
27	CTCTCCTGCTACAGCAGCCCGGCATTTCT <u>(SEQ ID NO: 34)</u>	3'Cy3	5'NH2 phospho- thioate
28	CGAAGGCAAAGCCCTTATGAACAGAGCAGC <u>(SEQ ID NO: 35)</u>	3'Cy3	5'NH2 phospho- thioate
29	TCCCAATGAATACACGGGAGTTCATGGAGC <u>(SEQ ID NO: 36)</u>	3'Cy3	5'NH2 phospho- thioate
30	GGATCTGTCTTGTTGGTAACGTTGCTGGCC <u>(SEQ ID NO: 37)</u>	3'Cy3	5'NH2 phospho- thioate
31	TCATCTTTCTTCACGGAGCTGCTGCTCTGC <u>(SEQ ID NO: 38)</u>	3'Cy3	5'NH2 phospho- thioate
32	TGGGTCAGCTCCTTCTTAATGGCCTGAAGG <u>(SEQ ID NO: 39)</u>	3'Cy3	5'NH2 phospho- thioate

33	AGAATTGAAGCCACTTTTGCCCCCTTCGTGA	3 'Cy3	5 'NH2 phospho-
	<u>(SEQ ID NO: 40)</u>		thioate
34	TACATTTGTGTTGAACTGCCCCACACAGCA	3 'Cy3	5 'NH2 phospho-
	<u>(SEQ ID NO: 41)</u>		thioate
35	TCAAAGGAAGTGAAAATGGGACTAGGCGCG	3 'Cy3	5 'NH2 Phospho-
	<u>(SEQ ID NO: 42)</u>		thioate
36	ATGTGCTTAAGAGTCATCCTCGCCATTGGC	3 'Cy3	5 'NH2 phospho-
	<u>(SEQ ID NO: 43)</u>		thioate
37	AGCTCTTTCAGCTGCTTCCTGCGTCTCAAA	3 'Cy3	5 'NH2 phospho-
	<u>(SEQ ID NO: 44)</u>		thioate
38	ACTCCACTTTTGCGAAGTGATGGATCACGC	3 'Cy3	5 'NH2 phospho-
	<u>(SEQ ID NO: 45)</u>		thioate
39	GAGACCACATGATGCGTACTGGCTTGCCCT	3 'Cy3	5 'NH2 phospho-
	<u>(SEQ ID NO: 46)</u>		thioate
40	TCAAAATTCATGGTGTCCAAAGCACGCTCC	3 'Cy3	5 'NH2 phospho-
	<u>(SEQ ID NO: 47)</u>		thioate
41	GCCGGCTGCTGGAAGTTCACATACGCGTAG	3 'Cy3	5 'NH2 phospho-
	<u>(SEQ ID NO: 48)</u>		thioate
42	TTCAAATTTGCGCTTAAGTTCCGTCTGCCG	3 'Cy3	5 'NH2 phospho-
	<u>(SEQ ID NO: 49)</u>		thioate
43	TTGAGCTCCTTTCCGTTCATCTCATCCACA	3 'Cy3	5 'NH2 phospho-
	<u>(SEQ ID NO: 50)</u>		thioate
44	AAGGCGCTCATCATCCATGTCTTCTCCAAA	3 'Cy3	5 'NH2 phospho-
	<u>(SEQ ID NO: 51)</u>		thioate
45	CATGACTCGTGGAACCTGTGAAGAAGCTGG	3 'Cy3	5 'NH2 phospho-
	<u>(SEQ ID NO: 52)</u>		thioate
46	ACTAAATGGTGGTCTAGGAGCAGCTGGGCG	3 'Cy3	5 'NH2 phospho-
	<u>(SEQ ID NO: 53)</u>		thioate
47	AGCACCGGGCATATTTTGAATGGATGAGG	3 'Cy3	5 'NH2 phospho-
	<u>(SEQ ID NO: 54)</u>		thioate
48	ACCCTGAGCAGTCCAGCGAGGACTTGGTCT	3 'Cy3	5 'NH2 phospho-
	<u>(SEQ ID NO: 55)</u>		thioate

49	CTACTCCTGCTGTCCGCACCGTTCCACAGT	3'Cy3	5'NH2 phospho-
	<u>(SEQ ID NO: 56)</u>		thioate
50	TGCAGGAGTTTCGCAATCCTCAGCAACATCT	3'Cy3	5'NH2 phospho-
	<u>(SEQ ID NO: 57)</u>		thioate
51	TGCACAGCCACAAGTTACAATGCAACAGCC	3'Cy3	5'NH2 phospho-
	<u>(SEQ ID NO: 58)</u>		thioate
52	TCAGGAACCTTTGACTGCTTCCATGTTGGC	3'Cy3	5'NH2 phospho-
	<u>(SEQ ID NO: 59)</u>		thioate
53	CCTCTGCAGACTACTATTAC	3'Cy3	5'NH2
	<u>(SEQ ID NO: 60)</u>		
54	CCTCTGCAGACTACTATTAC		5'NH2
	<u>(SEQ ID NO: 60)</u>		
55	CCTCTGCAGACTACTATTAC	3'Cy3	5'NH2 phospho-
	<u>(SEQ ID NO: 60)</u>		thioate

b) Production of the array

Please delete paragraph [0303] and replace it with the following paragraph:

[0303] Eight in vitro RNAs with the following sequence segments are used:

RNA 1: (SEQ ID NO: 61)

5'ucuagaaaauuuuuuguuuuacuuaagaaggagauauacauaugaaccccagugccccag
cuacccauggccucgcucuacgugggggaccuccaccccgacgugaccgaggcgaugcucuac
gagaaguucagcccggccggggcccauccucuccauccgggucugcaggggacaugaucacccgcc
gcuccuuggggcuacgcguaugugaacuuccagcagccggcgagcgugcuuuggacac
caugaauuuugauguuauaaagggaagccaguacgcaucauguggucucagcgugaucacauca
cuucgcaaaaguggaguaggcaacauauucauuuuuuuuuucuggacaaauccaugauaauaaag
cacuguaugauacauuuucugcuuuugguaacaucuuucauguaaggugguuugugaugaaaa
ugguuccaagggcuauuggauuuuguacacuuugagacgcaggaagcagcugaaagagcuauugaa

aaaugaauggaugcuccuaaaugaucgcaaaguauuuguuggacgauuaagucucguaaag
aacgagaagcugaacuuggagcuagggcaaaagaauuc3 '

RNA 2: (SEQ ID NO: 62)

5 'aacugcuuucugggcagccucuuuagcuuggugggcuuguaguacagcuacagcuucauaa
ccuugaacggagugacucugggagacucgagcauaugaagaaguucugaauuaucuaucuccaa
caacaugccagugauuuuaccagcaagaguagggugcauggcuugaauaagaggaaacagccgu
ucacccaacauuugcuuuugcucuuagaggagggcagaugccaacauggaagcagucuaaagguu
ccugaccuuguacaugaacagcaggcuguugcauuguaacuuguggcugugcauaaagauguug
cugaggauugcgaacuccugcagcauauuuauacuguggaacggugcggacagcaggaguagcu
gcagcggcugcagcugcaggacguggacccaugucuguguugauguguuagcaacacgcugug
uug3 '

RNA 3: (SEQ ID NO: 63)

5 'ucuagaaaaauaauuaguguuauagucuaaagauuuguuuucuaaaguug
auacuguggguuauuuuugugaacagccugauguuugggaccuuuuuuccuc
aaaauaaacaaguccuuauuaaaccaggaauuuggagaaaaaaaagggaauuc3 '

RNA 4: (SEQ ID NO: 64)

5 'gaauuccaaacccgggaguaggagacucagaaucgaaucucuucuccuccccuucuuuguga
gauuuuuuugaucuucagcuacauuuucggcuuugugagaaaccuuaccauaaacacgauggc
cagcaacguuaccaacaagacagauccucgcuccaagaacucccguguauucauugggaauuc
aacacucuuguggucaagaaaucugauguggaggcaaucuuuucgaaguauggcaaaaugugg
gcugcucuguucauaagggcuuugccuucguucaguauguuaaugagagaaaugcccgggcugc
uguagcaggagaggauggcagaaugauugcuggccagguuuuagauauuaaccugggcugcag3 '

RNA 5: (SEQ ID NO: 65)

5 'gaauucaccaauguuuacaucaagaauuuuggagaagacauggaugaugagcgccuaaagga
ucucuugggcaaguuuugggccugccuuaagugugaaaguaaugacugaugaaaguggaaaaucc
aaaggauuuggauuuugaagcuuugaaaggcaugaagaugcacagaaagcuguggaugagauga
acggaaaggagcucaauggaaaacaaauuuauuguuggucgagcucagaaaaagguggaacggca
gacggaacuuaagcgcaaaauugaacagaugaacaagauaggauaccagauaccaggguuu

aaucuuuaugugaaaaaucuugaugaugguauugaugaacgucuccggaaagaguuuucuc
cauuugguacaaucauag3`

RNA 6: (SEQ ID NO: 66)

5`agugcaaagguuaugauggaggguggucgcagcaaaggguuugguuuuguauguuuccuccuc
cccagaagaagccacuaaagcaguuaacagaaaugaacgguaagaauuguggccacaaagccauug
uauguagcuuuagcucagcgcaaagaagagcgccaggcucaccucacuaaccaguuauaugcaga
gaauggcaaguguacgagcuguuuccaaaccuguaaucaaccccuaccagccagcaccuccuuc
agguuacuuauggcagcuaucccacagacucagaaccgugcugcauacuauccuccuagccaa
auugcucaacuaagaccaaguccucgcuggacugcucagggugccagaccucauccauuccaaa
auaugcccggugcuauccgcccagcugcuccuagaccaccauuuaguacuaugagaccagcuuc
uucacagguuccacgagucauguc3`

RNA 7: (SEQ ID NO: 67)

5`cugcagcgggagauguacggcuccucuuuugacuuggacuaugacuuaacgggacuauuau
gauaggauguacaguuaaccagcacguguaccuccuccuccuccuauugcucgggcuguagugc
ccucgaaacgucagcguguaucaggaaacacuucacgaaggggcaaaaguggcuucaauucuaa
gaguggacagcggggauccuuccaagucuggaaaguugaaaggagaugaccuucaggccauuaag
aaggagcugacccagauaaaaacaaaaguggauucucuccuggaaaaccuggaaaaauugaaa
aggaacagagcaaacaagcaguagagaugaagaauugauaagucagaagaggagcagagcagcag
cuccgugaagaaagaugagacuaauugugaagauggagucugaggggggugcagaugacucugcu
gaggagggggaccuacuggaugaugaugauaauagaagauccggggggaugaccagcug3`

RNA 8: (SEQ ID NO: 68)

5`cagcuggaguugaucaaggauaugaaaaagaggcugaggaaggagaggaugacagagacag
cgccaauggcgaggaugacucuaaagcacauagugggguuuagaaaucuaucccauuuuuc
uuaccuaggcgcuugucuaagaucaaaauuuuuccaccagauccucuccccuaguaucuuucagcac
augcucacugucuccccauccuuguccuucccauguucauuauuacauauugccccgcgccua
gucccauuuuacacuuccuuugacgcuccuaguaguuuuuguaagucuuaccugaaaauuuugc
uuuuauuuuugauaccucuuuaugacuuuacaaauaaaaaggauguaugguuuuuaucaacuguc
uccaaaauaaauucucuuguuaugcagggaguacaguucuuuucauucuaacuaaaguucaguagu
ugcuucccuaacugcaaaggcaaucucauuuaguugaguagcucuugaaagcagcuuugaguua

gaaguauguguguuacacccucacauuagugugcuguguggggcaguucaacacaaauguaaca
auuauuuuugugaaugagaguuggcaugucaaaugcauccucuaga3'

e) Hybridisation of RNA

Please delete paragraph [0312] and replace it with the following paragraph:

[0312] On a four inch Borofloat wafer (PEG surface) modified with hydroxyl groups, the sequence (3'→5') TCT-ATA-TGG-CAG (SEQ ID NO: 69) was synthesised on an OligoPilotII (Pharmacia) by the standard phosphoramidite method while retaining the last DMT protective group. This was then removed at defined positions by deprotecting by means of a 128 µm mask (4 channels per chip). Subsequently, a dT amidite (DMT-ON) was coupled to the sites which had then become accessible for synthesis. Subsequently, the same 128 µm mask was used for again deprotection; however, its position was shifted by 256 µm in comparison with the first mask deprotection.

Please delete paragraph [0314] and replace it with the following paragraph:

[0314] To couple the cleavable 5'-(S-dimethoxytrityl)-mercapto-5'-deoxythymidine-3'-phosphoramidite (0,1 M solution), standard coupling protocols of the 1 µmol scale were modified: coupling time: 900 s, deblocking: 250 s, rinsing: 600 s with a 220 mM DTT solution in THF/pyridine/water (7/1/2). Subsequently, a dT-amidite was coupled, followed by the remaining sequence (3'→5') CAT-TCC-CGA (SEQ ID NO: 70) (deblocking, capping and oxidation corresponding to the standard protocol, 0.2 µmole scale). A solution with a lower iodine concentration (0.02 M iodine, Roth) was used for the oxidation step. To remove the base protective

Application No.: 10/789,081

Docket No.: MAIWAL 3.9-002 CONT

groups, the arrays were subsequently treated in 30-33% ammonia (Roth) for 35 min at 55°C.

Hybridisation